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The effect of positive end-expiratory pressure on optic nerve diameter in patients undergoing craniotomy operation

The effect of positive end-expiratory pressure on optic nerve diameter

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Abstract
Aim: In this study, we aimed to investigate the effect of PEEP on changes in intracranial pressure with the guidance of ultrasonographic measurement of the optic nerve, in patients who underwent craniotomy operation in the supine position.
Material and Methods: A total of 60 patients evaluated as ASA I-II and who were scheduled for craniotomy operation in the supine position under elective conditions were included in the study. Following routine monitorization of anesthesia induction, patients were provided with 1 mcg/kg iv fentanyl, 3 mg/kg iv thiopental sodium, 0.6 mg/kg iv rocuronium. Anesthesia maintenance was then provided with 2% sevoflurane and remifentanil (0,05-2 mcg/kg/min) infusion to keep BIS between 40 and 65. Patients in Group I received a 5 cmH_2O PEEP, while those in Group II received 0 cmH_2O PEEP. Patients' HR, SAP, DAP, MAP, end-tidal carbon dioxide ($ETCO_2$), SpO_2, Ppeak, Pmean, minute volume, Tv expiratory, ONSD values were measured at following time-points: T0-before anesthesia induction, T1-after the dura is opened, T2-immediately before the dura is closed, T3-before extubation.
Results: There was no statistical difference in hemodynamic parameters (SAP, DAP, MAP) between the two groups (p>0.05). ONSD was similar between both groups at all time points except for T2 results . The mean ONSD at T2 was significantly higher in Group I (p=0.04). Ppeak and Pmean were significantly higher in Group I at all time points (p<0.05).
Discussion: We investigated the effect of PEEP on the optic nerve sheath diameter and its indirect effect on intracranial pressure; we revealed that two different PEEP levels did not create a difference.

Keywords
Intracranial pressure; PEEP; Optic ultrasound

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Introduction

Intracranial hypertension may negatively affect patient outcomes in the perioperative period, as it leads to cerebral ischemia. On the other hand, the use of positive end-expiratory pressure (PEEP), recruitment maneuvers and prone position in order to prevent atelectasis in the intraoperative period may cause undesirable effects on cerebral physiology by decreasing cerebral venous return and mean arterial pressure. In addition, lung-sparing ventilation targets (airway plateau pressure <28-30 cmH_2O, driving pressure <14 cmH_2O or delta-transpulmonary pressures <10–12 cmH_2O) may cause hypercarbia, leading to changes in intracranial pressure [1]. It has been shown that continuous PEEP applications lower cerebral blood flow and cerebral perfusion pressure both in healthy volunteers and patients with cerebral damage [2]. However, recent studies have noted positive changes in intracranial pressure (ICP) in patients who received PEEP. PEEP opens collapsed alveoli, improving oxygenation. In this way, end-expiratory alveolar collapse is prevented, intrapulmonary shunting is reduced, functional residual capacity is increased, and the risk of developing complications such as ventilator mediated pneumonia or pulmonary damage is decreased in patients under general anesthesia [3].

The optic nerve, which is part of the central nervous system, is surrounded by a subarachnoid space containing the dural sheath and cerebrospinal fluid (CSF). Intense adhesion between the optic nerve and its sheath is observed in the posterior part of the nerve in the optic canal. However, the sheath is less adhered to the nerve in the anterior part and especially in the retrobulbar segment of the optic nerve, and is surrounded only by orbital fat. For this reason, the retrobulbar optic nerve sheath can be flexible and expanded in the case of increased pressure in the CSF [4]. Ultrasonographic measurement of the optic nerve sheath diameter (ONSD) is a simple, non-invasive and safe technique for evaluation of ICP. ONSD can be obtained by axial measurement 3 mm behind the optic nerve head using optical imaging performed with transorbital sonography [5] (Figure 1).

In this observational study, we aimed to investigate the effect of using PEEP on changes in intracranial pressure with the guidance of ultrasonographic measurement of the optic nerve, in patients who underwent craniotomy operation in the supine position.

Material and Methods

This prospective one-way, randomized controlled study was conducted after the approval of the Institutional Ethics Committee (decision no: 2019/514/147/3) according to the ethical principles outlined in the Helsinki Declaration and Guidelines for Good Clinical Practice. Written informed consent was obtained from all the participants.

Study population

A total of 60 female and male patients aged over 18 years, evaluated as ASA I-II and scheduled for craniotomy operation in the supine position under elective conditions were included in the study.

Exclusion criteria

Patients who had a surgical operation related to the optic nerve, those with a history of drug allergy, glaucoma or increased intraocular pressure, pregnant patients and those with retinal detachment were excluded from the study.

Anesthesia procedure

All patients were routinely monitored in the operating room with electrocardiography (ECG), noninvasive blood pressure, pulse oximeter (SpO_2) and bispectral index (BIS). Patients' heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), and mean arterial pressure were measured and recorded. In order to capture the best view between the retrobulbar echogenic adipose tissue and vertical hypoechoic band, a linear ultrasound probe running at 7.5 MHz (Toshiba Aplio 50 XV USG device) was inserted in the gel at the transverse plane horizontally, 3.0 mm behind the optic nerve by taking care not to apply pressure to the eyeball, and ONSD measurement was made and recorded while the eyelid was closed. Following preoxygenation, anesthesia induction was provided with 1 mcg/kg iv fentanyl, 3 mg/kg iv thiopental sodium, and 0.6 mg/kg iv rocuronium. Anesthesia maintenance was then provided with 2% sevoflurane and remifentanil (0,05- 2 mcg/kg/min) infusion to keep BIS between 40 and 65. Patients in Group I received a 5 cmH_2O PEEP, while those in Group II received 0 cmH_2O PEEP.

Data collection

Patients' HR, SAP, DAP, MAP, end-tidal carbon dioxide (ET CO_2), SpO_2, Ppeak, Pmean, minute volume ve Tv expiratory and ONSD values were measured at following time-points: T0- before anesthesia induction, T1- after the dura is opened, T2- immediately before the dura is closed, T3- before extubation.

Statistical Analysis

Results obtained in this study were statistically analyzed with IBM SPSS Statistics software version 22.0. The t-test was used in the comparison of the descriptive statistical parameters (mean, standard deviation, minimum and maximum values) between the two groups, and a one-way ANOVA test was used in multiple comparisons. P- values <0.05 were considered statistically significant.

Chiu et al. found reference ONSD values as 4.5 mm and maximum values as 5.1 mm [6]. As a result of the power analysis made, taking alpha error as 0.05, beta error as 0.20 and effect size as 0.70; the required minimum number of patients was calculated as 26 patients per group, 52 patients in total. Considering the possible losses during the study period, 30 patients per group, 60 patients in total were included in the study.

Results

A total of 60 patients were recruited in the study. Patients' characteristics are shown in Table 1. No significant difference was found between the groups in terms of HR, SAP, DAP, MAP and SpO_2 values measured at T0 (before anesthesia induction), T1 (after the dura is opened), T2 (immediately the dura is closed) and T3 (before extubation) time points ($p>0.05$).

ONSD was similar between both groups at all time points except for the results at T2. The mean ONSD at T2 was significantly higher in Group I ($p=0.04$). In the intragroup comparison, ONSD was significantly lower at T1 and T2 time points compared to before induction in both groups ($p<0.001$). ONSD dropped by 1.08 mm at T1 compared to before induction in both groups. ONSD was 1.19 mm lower at T2 in Group I, while this value

Table 1. Demographic features of the patients and comparison between the groups

	Total	Group I (n=30)	Group II (n=30)	p
Age (year)	55.0±10.8	53.2±10.9	56.8±10.5	0.196
Gender (M / F)	29 / 31	12 / 18	17 / 13	0.196
Height (cm)	167.0±8.6	168.0±8.6	166.1±8.7	0.402
Weight (kg)	76.1±12.5	78.9±12.8	73.3±11.7	0.092
ASA (I / II / III)	1 / 50 / 9	1 / 24 / 5	0 / 26 / 4	0.551
Comorbidity (%)	35 (58.3%)	16 (53.3%)	19 (63.3%)	0.432
History of Smoking (%)	34 (56.7%)	16 (53.3%)	18 (63.3%)	0.602
Increased intracranial pressure (%)	3 (5.0%)	2 (6.7%)	1 (3.3%)	1.000
Presence of CVP (%)	29 (48.3%)	16 (53.3%)	13 (43.3%)	0.438

Table 2. Comparison of ONSDs between themselves according to the groups and measurement times

ONSD (mm)	Group I	p	Group II	p
ONSD T0-T1	4.67±0.50 3.59±0.58	0,001*	4.42±0.66 3.44±0.62	0,001*
ONSD T0-T2	4.67±0.50 3.48±0.54	0,001*	4.42±0.66 3.17±0.63	0,001*
ONSD T0-T3	4.67±0.50 4.20±0.44	0,001*	4.42±0.66 4.09±0.64	0,075

*p<0.05 statistically significant

Table 3. Comparison of the respiratory parameters between the groups

	Group I	Group II	p
EtCO2 (mmHg)			
T1	31.9±4.1	31.0±3.3	0.265
T2	31.8±2.9	30.4±1.9	0.051
T3	31.7±2.8	30.7±2.3	0.194
Ppeak (cmH2O)			
T1	19.5±4.8	16.6±3.2	0.010*
T2	19.2±3.8	16.7±3.4	0.008*
T3	19.2±3.9	16.9±3.6	0.015*
Pmean (cmH2O)			
T1	8.76±1.00	7.13±0.93	<0.001*
T2	8.70±1.20	7.03±1.21	<0.001*
T3	8.66±1.09	7.30±1.14	<0.001*
MV(liter)			
T1	5.91±0.93	5.58±1.00	0.066
T2	5.85±1.18	5.36±0.63	0.157
T3	5.79±0.96	5.35±0.62	0.087
Tv expiratory (liter)			
T1	497.3±57.6	484.8±48.1	0.579
T2	496.9±55.7	484.6±46.5	0.605
T3	492.9±57.6	486.8±51.7	0.723

EtCO2: end tidal carbon dioxide, Ppeak: peak airway pressure, Pmean: average airway pressure,
MV: minute volume, Tv expiratory: expiratory tidal volume,
*p<0.05 statistically significant

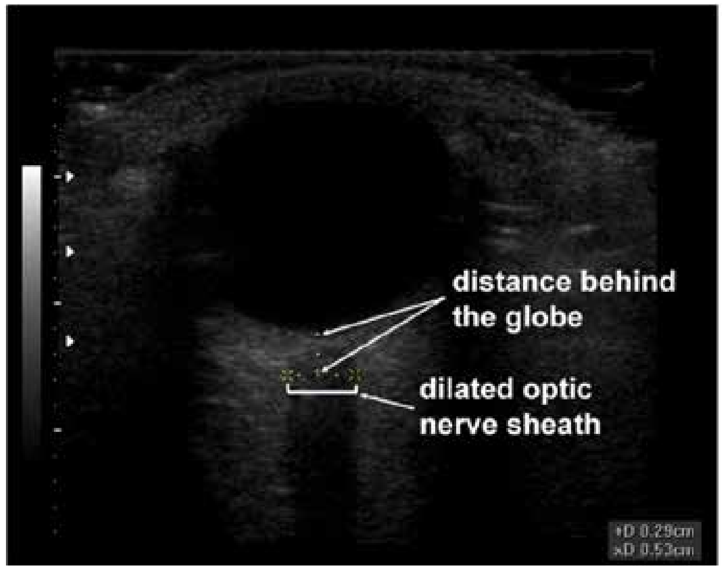

Figure 1. View of dilated optic nerve sheath by ocular sonography

was 1.35 mm in Group II. ONSD was significantly lower at T3 compared to T0 in Group I (p<0.001), while there was no significant difference between these time points in Group II (p=0.075). ONSD dropped by an average of 0.47 mm at T3 in Group I, while this value was 0.33 in Group II (Table 2).

When among respiratory parameters $EtCO_2$, Ppeak, Pmean, minute volume and Tv expiration were evaluated, Ppeak and Pmean were significantly higher in Group I at all time points (p<0.05), but no significant difference was observed between the groups in terms of the other parameters (Table 3).

Whereas a statistically significant correlation was found between ONSD and mean arterial pressure values measured at T0 (before anesthesia induction) and T2 (immediately before the dura was closed) (p=0.02), no significant correlation was found between parameter measurements in Group II.

Discussion

Measurement of optic nerve sheath diameter is quite adequate and well-standardized compared to other complex ultrasonographic measurement methods, and the results can be readily measured again for check. Tayal et al. [7] showed that physicians who had no ocular ultrasonography experience previously became qualified by performing 25 ONSD measurements. There may be a risk of subjective data measurement depending on the person who performs the measurement. Therefore, in our study, all measurements were made by the same person experienced in ONSD measurement. In this way, we tried to standardize the increase and decrease of the measurements. Blaivas et al. reported that they have used ocular USG in adult patients in the emergency department with suspicion of elevated intracranial pressure. They suggested this method as a rapid, bedside and noninvasive way of determining increased intracranial pressure in case of alterations in the level of consciousness [8].

Normal ICP varies between 7 and 15 mmHg in adults in the supine position. ICP over 15 mmHg is considered abnormal, and over 20 mmHg is considered pathological. Increased ICP during anesthesia may be seen with laryngoscopy, pneumoperitoneum a high PEEP, upright Trendelenburg position, low anesthesia status and extubation [9].

Muench et al. [10], investigating the effect of different PEEP levels (0-10 cmH_2O) on intracranial pressure, cerebral oxygenation, regional cerebral blood flow and systemic hemodynamic variable, and found that increased PEEP caused significant decreases in mean arterial pressure and cerebral blood flow. However, the authors stated that the change in cerebral blood flow was essentially dependent on the change in mean arterial pressure, and brain perfusion did not impair when mean arterial pressure kept stable.

In a retrospective study investigating patients with severe neurologic injury (GCS<9) who required ICP monitoring, no significant correlation was found between PEEP or ICP or cerebral perfusion pressure (CPP), except for patients with severe pulmonary injury. In the multivariate analysis of patients with severe pulmonary injury, each 1 cmH_2O increase in PEEP was found to be correlated with a 0.31 mmHg increase in ICP (p=0.04) and 0.85 mmHg decrease in CPP (p=0.002) [11].

In our study, a 5 mmHg PEEP was applied in Group I, while no PEEP was administered in Group 2. Increased PEEP values were not needed, as there was no change or deterioration in the situation related to respiratory functions, and in conclusion, deep and prolonged hypotension was not noted in any patient. HR, SAP, DAP, MAP and SpO_2 values were within normal limits at all time points, and in both groups, the differences were not statistically significant. This normotensive situation provided stable perfusion pressure, while there was a difference between the groups only in ONSD measurements at T2 (immediately before the dura is closed) time point. However, we think that this was not at a level that can create a clinical impact.

On the other hand, in a prospective study including 21 intensive care patients with normal and abnormal lung compliance, the effects of increases in PEEP on central venous pressure (CVP), CPP, ICP and cerebral compliance were studied. In patients with normal compliance, increased PEEP caused an increase in CVP and a decrease in mean arterial pressure and CPP, while ICP and cerebral compliance did not change. Whereas, in patients with low compliance the increase in PEEP did not create any change in the variables [12].

In a prospective, single-center study including 499 patients with brain injury, including subarachnoid hemorrhage, it was reported that low tidal volumes and higher PEEP caused mechanic ventilation duration to drop to 12.6 days from 14.9 days and a 90-day length of stay in intensive care unit on average [13]. In a multi-center study on patients with acute cerebral injury, including subarachnoid hemorrhage, low tidal volume (<7 ml/kg), moderate PEEP (6-8 cmH2O), and early extubation protocol were associated with mortality and a decrease in the number of invasive ventilation free days [14]. In a single-center study examining the relationship between lung-sparing ventilation and ICP, ICP values of 12 subarachnoid hemorrhage patients with hypercapnia ($PaCO_2$ 50-60 mmHg) who were ventilated with lung- sparing ventilation modes were not higher than ICP values of the patients with a $PaCO_2$ value of 40 mmHg [15].

In a study by Mehrpaur et al. [16], ONSD measurement with ultrasonography was demonstrated as an effective non-invasive method for the determination of intracranial hypertension. Rajajee et al. [17], measured ONSD in a group of 536 patients with head trauma, ischemic stroke and cranial tumors, and found that increased ICP values were correlated with the changes in ONSD. Again in the same study, the optimal cut-off value for ICP >20 mmHg was reported as 4.8 mm for both eyes with 86% sensitivity and 94% specificity rates. Hamilton et al. found that with an increase in ICP for every 1 mm Hg, ONSD increased by 0.0034±0.0003 mm [18].

Special attention is recommended in the adjustment and monitoring of airway pressures and minute ventilation when mechanical ventilation is required in patients with brain injury [19] because, regardless of the ventilation adjustment, according to the basic conditions of cerebral autoregulation, it can affect ICP positively or negatively in a neurocritical patient depending on the final results on PaO_2 and ICP.

In our study, Ppeak and Pmean (5 cmH_2O PEEP) were significantly higher at all time points in Group I (p<0.05); however, there was no significant difference between the groups in terms of the other respiratory parameters. Furthermore, there was no significant difference between the groups in terms of ONSD value except for the T2 time point.

In a study investigating the effect of upside- down position on ICP in awake and anesthetized rabbits, it was shown that after a small increase, ICP gradually increasedin the first 12 hours in the awake rabbits, whereas ICP gradually decreased in the 8 hours following a marked increase in the anesthetized rabbits. This indicated that fluid shift and venous expansion have at least as much effect as impairment of cerebral venous drainage on the increase of ICP [20]. Accordingly, it can be predicted also in humans that ICP will increase faster in an anesthetized patient compared to an awake one. Therefore, the anesthetic agent to be chosen should provide sufficient cerebral perfusion pressure, while ICP should not cause fluctuations in cerebral blood flow and cerebral oxygen demand. Sujata et al. [21] compared the effects of propofol on ONSD and ICP, and Chui et al. [6] effects of propofol and volatile anesthesia in craniotomy procedures. Both studies showed that the effects on brain relaxation score were similar, despite the fact that the mean ICP values were lower and CPP values were higher with propofol maintenance. In our study, balanced anesthesia was achieved in all patients in the supine position with sevoflurane, and no significant difference was found between the group in ONSD except for the T2 time point.

In a recent study, Robba et al. evaluated the changes in ICP caused by the prone position or PEEP in patients undergoing spinal surgery and showed that prone position and PEEP >8 mmH_2O increased the mean ONSD value [22]. On the other hand, a high PEEP level has been shown to create an important difference in ICP when applied in ARDS patients with cerebral damage [23]. However, it is not known which PEEP level is the most appropriate for patients with acute brain injury [24].

Although invasive ICP measurement remains the gold standard, these methods (Doppler and ONSD) can be easily used in patients with hemostatic disorders when invasive devices are not indicated (such as mild traumatic brain injury) [25].

Study Limitations

Minimum limit values of the optic nerve sheath diameters that show the increase in ICP are not clear, as specified in previous studies. However, previous studies have shown that ONSD is correlated with ICP and can be used in the determination of ICP in various clinical situations.

Another limitation is the risk of subjective data that may occur during the measurement and depend on the person who measures the values.

Conclusion

In this study, in which we investigated the effect of PEEP on the optic nerve sheath diameter and its indirect effect on intracranial pressure, we revealed that two different PEEP levels did not create a difference. Ultrason guided ONSD is a noninvasive monitoring tool for a brain- protective ventilation strategy in neurocritical patients in need of mechanical ventilation when invasive monitoring of ICP is not indicated, can not be accessed, or contraindicated.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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